

DECLARATION UNDER 37 C.F.R §1.132

I, Brian R. Genge, declare as follows:

I am a U.S. citizen, and I presently reside at 2814 Montgomery St., Columbia, SC 29205. I am an inventor of the subject matter of U.S. Patent Application Serial No. 09/978,601, the patentability of which is presently at issue. I am presently employed by the University of South Carolina, and my position is Research Associate Professor, Department of Chemistry and Biochemistry. I hold a B.S. degree in chemistry from the University of Wisconsin, and a Ph.D. in biochemistry from the University of South Carolina. I have been active in the field of biomaterials and biochemical research for the past ten years and I am the author of 40 publications covering various aspects of that field.

The information provided below describes laboratory tests that were carried out in my laboratory at the University of South Carolina to determine the compressive strength of a cement material that was produced according to the methods taught in U.S. Patent 5,149,368 to Liu, *et al.*, issued September 22, 1992, titled *Resorbable bioactive calcium phosphate cement*

. The purpose of the tests was to enable a direct comparison between the compressive strength of a calcium phosphate cement made according to the methods taught in the Liu *et al.* patent and a cement made by the method taught in my pending patent application.

Production of tetracalcium phosphate:

Tetracalcium phosphate was prepared from a homogenous mixture having a Ca/P ratio of 2, or slightly less than 2, according to the method of Chow, et al. (U. S. Patent No. 5,522,893). The starting material consisted of 1.0 moles of CaHPO_4 (136 grams) and 0.9 moles of CaCO_3 (90 grams) that were combined, mixed and ground together using a Retsch Mixer Mill using zirconia grinding media. The mixture was then packed into a high temperature alumina crucible and heated to 1450 degrees Celsius in a Thermolyne furnace, and the sample was maintained at that temperature for 12 hours, to assure as complete conversion as possible of the starting mixture to tetracalcium phosphate. The sample was removed from the furnace and the sintered material was

rapidly coarsely ground and simultaneously cooled by being crushed in a stainless steel pan with a solid 1 inch stainless steel rod. The temperature rapid dropped from 1450 Celsius to room temperature within 2 minutes. The coarsely ground material was then transferred to a Retsch Mixer Mill and finely ground to less than 5 microns (the 270 mesh as described in the Liu *et al.* patent would allow particle of less than 53 microns to pass through).

OUR EXAMPLE 1: (Performed as described by Liu et al., EXAMPLE 1.)

The pure tetracalcium phosphate prepared by the solid state reaction described above was ground to 270 mesh. A weighed sample (2 g) of the powder was mixed with 0.3 g of anhydrous citric acid using a Brinkmann 2000 mixer mill. The mixed powder was then further mixed manually in an agate mortar and pestle with 0.7 ml pure water, and formed a paste. This paste set within several minutes. This hardened paste was placed into Delrin molds to form round 9.8 mm diameter by 6.8 mm height cylinders. After 10 minutes at 37 degrees Celsius, the cylinders were removed from the molds, then further aged in pure water at 37 degrees Celsius. After 24 hours the compressive strength of the cylinders was tested using a Shimadzu Autograph AGSH-1 compression tester. The compressive strength of the cylinders ($n = 3$) was 3.06 ± 2.11 MPa.

OUR EXAMPLE 2: (Performed as described by Liu et al., EXAMPLE 4.)

In Example 1, the setting reagent used was pure citric acid. For Liu Example 4, in order to reduce the acidity of the setting reagent, the acidic citrate salts such as sodium citrate was used to replace citric acid as the setting reagent. For our Example 2, a sample of 2.0 grams of pure tetracalcium phosphate was premixed with 0.15 g $\text{Na}_3\text{citrate}$ and 0.15 g of anhydrous citric acid. This premixed powder was then intermixed with enough water to form a homogeneous mixed paste (720 μl). After several minutes, the paste hardened. This hardened paste was placed into Delrin molds to form round 9.8 mm diameter by 6.8 mm height cylinders. After 10 minutes at 37 degrees Celsius, the cylinders were removed from the molds, then further aged in pure water at 37 degrees Celsius. After 24 hours the compressive strength of the cylinders was tested using a Shimadzu Autograph AGSH-1 compression tester. The compressive strength of the cylinders ($n = 3$) was 7.53 ± 4.46 MPa.

Comparison with the compressive strength of cement made by the method described in our present patent application:

In Examples 1 - 5 of the present patent application, we show how to make a biocompatible cement that cures quickly and rapidly develops a high compressive strength. In Figure 3, in fact, the compressive strength of our material is shown to be about 50 MPa at the end of one hour, and to develop a compressive strength of over 90 MPa after 11 hours. The compressive strength at 24 hours would be expected to be even higher. By way of comparison, cements made according to the methods describe by Liu *et al.* were measured to have compressive strengths that ranged from about 1.4 MPa to about 11.6 MPa (3.06 ± 2.11 MPa and 7.53 ± 4.46 MPa)

In conclusion, it is evident that cement made by the methods described in U.S. Patent No. 5,149,368 to Liu *et al.*, have much lower compressive strength than a cement that is made according to the methods that we disclose in our application.

I declare that all statements herein made of my own knowledge are true and that all statements made herein on information and belief are believed to be true. I do hereby state that I am aware that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. §1001) and may jeopardize the validity of the application or any patent issuing thereon.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed on: 8-20-03 (Date)

Signature: Brian R. Genge
Brian R. Genge